Book Reviews

This new feature was recently added to *Current Separations* to broaden our scope by adding reviews of books and journals not only about our favorite topics such as electrochemistry, *in vivo* research, chromatography, CNS, diabetes and other science-related subjects, but also books on any number of subjects that our readers believe to be interesting and worthy of attention, books such as historical novels, biographies and mysteries. We encourage all of our readers to contribute reviews of books and journals you would like to share. Send them to *alice@bioanalytical.com*.

Handbook of Microdialysis, Ben H.C. Westerink and Thomas I.F.H. Cremers, Editors, 712 pp., $149.95, ISBN 978-0-444-52276-4, Amsterdam, The Netherlands, Academic Press, 2007.

This is a very impressive effort. Handbook is an understatement. Encyclopedia, Bible or "Harry Potter Does Microdialysis" would be better descriptions, but we all know the modesty Dutchmen can exhibit. Drs. Westerink and Cremers of the University of Groningen did yeoman's work in arm twisting participants to come up with 36 chapters in 697 pages. While $149.95 is not a price a Dutchman (or a Scotsman) would ever pay, it strikes me as very reasonable given the niche activity that microdialysis remains and the quality and mass of this very well produced volume.

This is not a how-to-do-it laboratory manual by any means, but rather is a fine progress report on how far microdialysis has come as a technique over 35 years and what we can do with it in preclinical and clinical pharmacology. The chapters are quite up to date with literature citations. Some chapters are broad overviews; some are molecule-centric, while others are disease-centric. There is good coverage of bioanalytical methodology and complementary techniques which add decision-making power.

I want to be transparent on three points: (1) One of the chapters is mine; (2) I've not read all the others; and (3) Our sales of BASi microdialysis products are progressing very nicely. Keeping these caveats in mind, this book will be of great value to any laboratory doing microdialysis today or contemplating doing so tomorrow. (Peter T. Kissinger)

The Demon under the Microscope, by Thomas Hager (352 pp., $24.95, ISBN 978-1-4000-8213-1, New York, NY, Crown Publishing Group, 2006)

The history of the science-based pharmaceutical industry is quite short. For all practical purposes, very little happened before 1900, and not a whole lot before 1950, except for a few important events that involved a small number of fascinating characters. One of the most prominent, no doubt, is the German physician and Nobel Prize laureate Gerhard Domagk. The story is messy, interwoven in complex ways with two world wars and a regulatory climate that had not kept pace with the developing science. As with most technological developments, there are many characters, the majority of whom get no credit and have faded from memory.

This is the story of the discovery, development, commercialization, and then decline, of sulfa drugs in the years from 1930 to 1950. In 1930 there were no effective synthetic antimicrobials; by 1950 there were many, with an established process for finding many more. For perspective, one might think of cellular telephones in 1980 versus 2000, from nothing to prevalent.

Sulfa drugs changed everything. They resulted from screening a library of compounds in vitro and in vivo. Their development involved cooperation of synthetic chemists and biologists with microscopes and mice and defined "medicinal chemistry" as we know it today, which evolved from the German dye industry. The very notion that one could make an organic chemical in a lab and cure a disease was as foreign then as genetic engineering has seemed more recently. Very few laboratories attempted it and the atmosphere was one of "this can't work, don't try" in an environment in the late 1920s and early 1930s that was very averse to R&D spending. As is the case today, the patent system influenced decisions, and a twist of metabolic fate made the unpatentable sulfanilamide a generic before its precursor Prontosil had gained full traction. Today we would call Prontosil a prodrug for sulfanilamide. Many variants on the theme were synthesized in an attempt to get economic advantage.

Clinical trials were hit-and-miss affairs. Formulations were not controlled or regulated, and 107 people died in the U.S. in 1937 when one manufacturer prepared an oral formulation in sweet-tasting, raspberry-flavored syrup made largely of diethylene glycol, a solvent that we now know destroys human kidneys. There was no trial, no approval of the formulation and clearly no common sense whatsoever. Imagine the unimaginable concept of making a batch and shipping it to pharmacists without further ado. The appropriate result was the Food, Drug and Cosmetic Act of 1938 which then influenced regulations in country after country, saving humanity much grief.

Compared to the volume also reviewed here, this one deals far more with context and focuses on an earlier time. It is fair to say that the seeds of all we argue about today were already planted. What is safe enough? What is effective enough? Who should make the money? What is the role of government?

Sulfa drugs have saved millions of people. How they came about is a fascinating tale well told here by Thomas Hager. (Peter T. Kissinger)

The Body Hunters, by Sonia Shah (256 pp., $24.95, ISBN 978-1-56584-912-9, New York, NY, The New Press, 2006)

When I am asked to describe drug development these days, I go into seminar mode and mention the tensions among five elements: (1) sick people and their families; (2) Wall Street; (3) pharmaceutical industry employees, including supporting vendors; (4) governments; and (5) academic science/medicine. This amounts to ten conflicting interactions with many ambiguities. I'll spare you my seminar, but consider a few of these tensions:

- *Wanting drugs faster versus wanting drugs to be safer.*
- *Wanting a high return on R&D invested versus*

wanting low drug prices.
- *Doing good versus doing harm with drugs.*
- *Approving drugs quickly versus being absolutely sure they are both safe and effective.*

Each of these elements has a different set of goals and incentives.

This book fits the genre of investigational journalism and by definition will annoy many. It goes over inconvenient truths that many of us in science, medicine and business know but are motivated to ignore out of frustration. It adds a sixth element to the above matrix – participants in clinical trials, particularly those in third world countries who have no access to treatment with a current standard of care. Many of these individuals are ill equipped to understand or afford any treatment. What does informed consent mean to individuals who need money for food and understand nothing of biology, pharmacology or statistics? Is a placebo-controlled trial appropriate in denying care to 50% of the subjects, or is it acceptable given that 100% of the subjects would otherwise have received no care at all, coupled with the fact that the 50% who receive the experimental drug are not guaranteed a positive outcome in any case? Is it perhaps a positive thing that all participants have access to a clinic and will receive care, and even food, not otherwise available to them? Or are the financial rewards to doctors, patients, clinics (new buildings, new equipment) and governments clouding all decisions?

The problem with a book such as this is that it presents one example after another of problems, many involving financial conflicts, moral dilemmas, and human failings. It presents nothing of what has been done well to the benefit of global healthcare. The virtue of an exposé is that it reminds us of the many challenges presented to us by biology. It will have been a positive contribution if the public recognizes the difficulties and sees the world of drug development as it really exists rather than as some ideal that does not. No doubt we are uncomfortable with what we don't know and can't know. We need to respond to comments such as, "Why didn't the company know that two people out of 30,000 would die? They should certainly have known this!" The fact that there are unknown unknowns is the reason we do clinical trials in the first place. It is research, and it is called a trial for a reason.

The point of view expressed in this book does have real value, however. Life science researchers should know this perspective and be humbled by it to do better. Denying there are issues is the wrong response. On the other hand, ignoring the many things that have gone right is just as inappropriate. Let's face it, reality is uncomfortable. Wishing it were something else does not make it so. Buy the book. It's a quick read. (Peter T. Kissinger)

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